We Claim:

1. A method for attenuating expression of a target gene in cultured cells, comprising introducing double stranded RNA (dsRNA) into the cells in an amount sufficient to attenuate expression of the target gene, wherein the dsRNA comprises a nucleotide sequence that hybridizes under stringent conditions to a nucleotide sequence of the target gene.

2. A method for attenuating expression of a target gene in a mammalian cell, comprising

   (i) activating one or both of a Dicer activity or an Argonaut activity in the cell, and

   (ii) introducing into the cell a double stranded RNA (dsRNA) in an amount sufficient to attenuate expression of the target gene, wherein the dsRNA comprises a nucleotide sequence that hybridizes under stringent conditions to a nucleotide sequence of the target gene.

3. The method of claim 2, wherein the cell is suspended in culture.

4. The method of claim 2, wherein the cell is in a whole animal, such as a non-human mammal.

5. The method of claim 1 or 2, wherein is engineered with (i) a recombinant gene encoding a Dicer activity, (ii) a recombinant gene encoding an Argonaut activity, or (iii) both.

6. The method of claim 5, wherein the recombinant gene encodes a protein which includes an amino acid sequence at least 50 percent identical to SEQ ID No. 2 or 4 or the Argonaut sequence shown in Figure 24.

7. The method of claim 5, wherein the recombinant gene includes a coding sequence hybridizes under wash conditions of 2 x SSC at 22°C to SEQ ID No. 1 or 3.

8. The method of claim 1 or 2, wherein an endogenous Dicer gene or Argonaut gene is activated.

9. The method of claim 1 or 2, wherein the target gene is an endogenous gene of the cell.

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10. The method of claim 1 or 2, wherein the target gene is an heterologous gene relative to the genome of the cell, such as a pathogen gene.

11. The method of claim 1 or 2, wherein the cell is treated with an agent that inhibits protein kinase RNA-activated (PKR) apoptosis, such as by treatment with agents which inhibit expression of PKR, cause its destruction, and/or inhibit the kinase activity of PKF.

12. The method of claim 1 or 2, wherein the cell is a primate cell, such as a human cell.

13. The method of claim 1 or 2, wherein the dsRNA is at least 20 nucleotides in length.

14. The method of claim 13, wherein the dsRNA is at least 100 nucleotides in length.

15. The method of claim 1 or 2, wherein expression of the target gene is attenuated by at least 10 fold.

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16. An assay for identifying nucleic acid sequences responsible for conferring a particular phenotype in a cell, comprising

(i) constructing a variegated library of nucleic acid sequences from a cell in an orientation relative to a promoter to produce double stranded DNA;

(ii) introducing the variegated dsRNA library into a culture of target cells, which cells have an activated Dicer activity or Argonaut activity;

(iii) identifying members of the library which confer a particular phenotype on the cell, and identifying the sequence from a cell which correspond, such as being identical or homologous, to the library member.

17. A method of conducting a drug discovery business comprising:

(i) identifying, by the assay of claim 16, a target gene which provides a phenotypically desirable response when inhibited by RNAi;

(ii) identifying agents by their ability to inhibit expression of the target gene or the activity of an expression product of the target gene;

(iii) conducting therapeutic profiling of agents identified in step (b), or further analogs thereof, for efficacy and toxicity in animals; and

(iv) formulating a pharmaceutical preparation including one or more agents identified in step (iii) as having an acceptable therapeutic profile.

18. The method of claim 17, including an additional step of establishing a distribution system for distributing the pharmaceutical preparation for sale, and may optionally include establishing a sales group for marketing the pharmaceutical preparation.

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19. A method of conducting a target discovery business comprising:
(i) identifying, by the assay of claim 16, a target gene which provides a phenotypically desirable response when inhibited by RNAi;
(ii) (optionally) conducting therapeutic profiling of the target gene for efficacy and toxicity in animals; and
(iii). licensing, to a third party, the rights for further drug development of inhibitors of the target gene.

20. A method for attenuating expression of a target gene in a cell, comprising introducing into the cell a hairpin nucleic acid in an amount sufficient to attenuate expression of the target gene, wherein the hairpin nucleic acid comprises an inverted repeat of a nucleotide sequence that hybridizes under stringent conditions to a nucleotide sequence of the target gene.

21. A hairpin nucleic acid for inhibiting expression of a target gene, comprising a first nucleotide sequence that hybridizes under stringent conditions to a nucleotide sequence of the target gene, and a second nucleotide sequence which is an complementary inverted repeat of said first nucleotide sequence and hybridizes to said first nucleotide sequence to form a hairpin structure.

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22. The method of claim 20 or the hairpin nucleic acid of claim 21, wherein the hairpin nucleic is RNA.

23. A non-human transgenic mammal having germline and/or somatic cells comprising a transgene encoding a dsRNA construct.

24. The transgenic animal of claim 23, which is chimeric for said transgene.

25. The transgenic animal of claim 23, wherein said transgene is chromosomally incorporated.

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